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PATENT COOPERATION TREATY

PCT/GB00/01

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING
OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

HARDING, Charles, Thomas
D. Young & Co.
21 New Fetter Lane
London EC4A 1DA
ROYAUME-UNI

Date of mailing (day/month/year) 21 August 2001 (21.08.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference P8690WO CTH	
International application No. PCT/GB00/01211	International filing date (day/month/year) 30 March 2000 (30.03.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address KING'S COLLEGE LONDON Strand London WC2R 2LS United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☒ the person ☐ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address OXFORD BIOMEDICA (UK) LIMITED Medawar Centre Robert Robinson Avenue The Oxford Science Park Oxford, OX4 4GA United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☐ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer QIU Anman Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 08 December 2000 (08.12.00)	
International application No. PCT/GB00/01211	Applicant's or agent's file reference P8690WO CTH
International filing date (day/month/year) 30 March 2000 (30.03.00)	Priority date (day/month/year) 31 March 1999 (31.03.99)
Applicant MADEN, Malcolm et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 20 October 2000 (20.10.00)

☐ in a notice effecting later election filed with the International Bureau on:

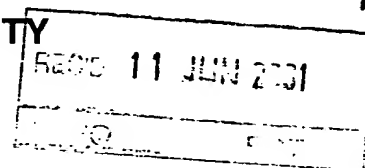
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Olivia TEFY Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P8690WO CTH	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/01211	International filing date (day/month/year) 30/03/2000	Priority date (day/month/year) 31/03/1999
International Patent Classification (IPC) or national classification and IPC A61K38/17		
Applicant KING'S COLLEGE LONDON et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 20/10/2000	Date of completion of this report 07.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Didelon, F Telephone No. +49 89 2399 7332 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01211

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-65 as originally filed

Claims, No.:

1-9 as originally filed

Drawings, sheets:

1/17-17/17 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/01211

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 5-8 (with respect to industrial applicability).

because:

- ☒ the said international application, or the said claims Nos. 5-8 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 7, 8

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

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	No:	Claims	1-6, 9
Inventive step (IS)	Yes:	Claims	7, 8
	No:	Claims	1-6, 9
Industrial applicability (IA)	Yes:	Claims	1-4, 9
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01211

Comments on item III:

Claims 5-8 relate to methods of treatment of the human/animal body which is subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Comments on item V:

1. Reference is made to the following documents:

D1: MADEN M ET AL: 'Retinoic acid as a chemotactic molecule in neuronal development.' INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE, vol. 16, no. 5, August 1998 (1998-08), pages 317-322, XP000946687 ISSN: 0736-5748 cited in the application

D2: MADEN M ET AL: 'RETINOIC ACID AND DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM' BIOESSAYS, vol. 14, no. 7, 1992, pages 431-438, XP002149699 ISSN: 0265-9247

D3: WO 97 24116 A (ALLERGAN INC) 10 July 1997 (1997-07-10)

D4: US-A-4 808 630 (STRAW GREGORY M) 28 February 1989 (1989-02-28)

2. The present application does not meet the requirements of Article 33(2) PCT because the subject matter of claims 1-6, 9 would not be considered as novel.

2.1 The subject-matter of claims 1 and 2 does not appear to be novel in view of the disclosures of D1 and D2 which relate to the positive action of retinoic acid on neurite outgrowth.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01211

2.2 Claims 1-6 and 9 are anticipated by the divulgation of D3 describing the use of retinoic acid in the treatment of psychotic disorders like schizophrenia (see column 2, lines 49-50, column 3, lines 13-18 and example 7).

Document D4 reveals in a similar manner that retinoid compounds can be used for the treatment of neurodegenerative diseases and other neurological disorders (see page 2, lines 22-31) .

3. The present application does not meet the requirements of Article 33(3) PCT because the subject-matter of claims 1-6, 9 lack an inventive activity.

Document D2 discloses that retinoic acid has a role in neurite outgrowth and in the development of the Central Nervous System (CNS). In addition , it is further suggested page 437, column 2, lines 7-12 that the use of retinoic acid would have profound medical implications, e.g in neuronal regeneration.

4. The implication of RAR β 2 receptor , associated with specific agonists like CD2019 (differing from the aspecific retinoic acid), in neuronal growth and development was not known so far. The use of RAR β 2 (with or without specific agonists like CD2019) for the treatment of neurological disorders (claims 7 and 8) seems therefore to be novel and to involve an inventive activity.

5. For the assessment of the present claims 5-8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01211

Comments on item VII:

The description page 14, lines 11-13, refers to "transgenic organism", including "any organism". Since it does not exclude human beings, this passage might be objected to in certain Contracting States under Rule 9.1 (i) PCT.

Comments on item VIII:

Claims 1, 8 and 9 lack clarity in the sense of Article 6 PCT since the expression "to cause neurite development" does not define a disorder to treat, but instead appears to be a result to be achieved and thus does not precisely the subject-matter of said claims. Instead, the diseases to be treated should be clearly designated.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 October 2000 (05.10.2000)

PCT

(10) International Publication Number
WO 00/57900 A3

(51) International Patent Classification⁷: **A61K 38/17**,
31/203, 31/381, 48/00, A61P 25/00

(74) Agents: **HARDING, Charles, Thomas et al.**; D. Young
& Co., 21 New Fetter Lane, London EC4A 1DA (GB).

(21) International Application Number: **PCT/GB00/01211**

(22) International Filing Date: **30 March 2000 (30.03.2000)**

(25) Filing Language: **English**

(26) Publication Language: **English**

(30) Priority Data:
9907461.9 31 March 1999 (31.03.1999) **GB**

(71) Applicant (for all designated States except US): **KING'S
COLLEGE LONDON [GB/GB]**; Strand, London WC2R
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(72) Inventors; and

(75) Inventors/Applicants (for US only): **MADEN, Malcolm**
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Institute, Developmental Biology Research Centre, King's
College London, 26/29 Drury Lane, London WC2B 5RL
(GB).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE,
DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— With international search report.

(88) Date of publication of the international search report:
15 February 2001

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **FACTOR FOR REGULATION OF NEURITE GROWTH**

(57) Abstract: The present invention relates to the use of RAR β 2 and/or an agonist thereof in the preparation of a medicament to cause neurite development.

WO 00/57900 A3

INTERNATIONAL SEARCH REPORT

In ational Application No
PCT/GB 00/01211

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/17 A61K31/203 A61K31/381 A61K48/00 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ, MEDLINE, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 23070 A (LIGAND PHARM INC) 1 August 1996 (1996-08-01) the whole document ---	1-9
A	JOHNSON A T ET AL: "IDENTIFICATION OF RETINOIC ACID RECEPTOR BETA SUBTYPE SPECIFIC AGONISTS" JOURNAL OF MEDICINAL CHEMISTRY, US, AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 39, no. 26, 20 December 1996 (1996-12-20), pages 5027-5030, XP002065588 ISSN: 0022-2623 the whole document --- -/--	2,6,8



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

10 October 2000

Date of mailing of the international search report

26/10/2000

Name and mailing address of the ISA

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Authorized officer

Stein, A

INTERNATIONAL SEARCH REPORT

In. ational Application No

PCT/GB 00/01211

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 02030 A (AMMAR KHODOR) 23 January 1997 (1997-01-23) page 8, line 20 -page 9, line 11 page 15, line 8 -page 18, line 15 claim 29 ---	3-6
A	WO 97 24116 A (ALLERGAN INC) 10 July 1997 (1997-07-10) the whole document, especially claims 1,2,5,12,13 ---	3-6
A	US 4 808 630 A (STRAW GREGORY M) 28 February 1989 (1989-02-28) the whole document ---	3,5,6
A	MADEN M ET AL: "Retinoic acid as a chemotactic molecule in neuronal development." INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE, vol. 16, no. 5, August 1998 (1998-08), pages 317-322, XP000946687 ISSN: 0736-5748 cited in the application the whole document ---	1-6,9
A	MADEN M ET AL: "RETINOIC ACID AND DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM" BIOESSAYS, vol. 14, no. 7, 1992, pages 431-438, XP002149699 ISSN: 0265-9247 the whole document ---	1-6,9
A	HAN, GUANGYANG ET AL: "Enhanced potency of 9-cis versus all-trans-retinoic acid to induce the differentiation of human neuroblastoma cells" DIFFERENTIATION (BERLIN) (1995), VOLUME DATE 1995, 59(1), 61-9 , XP000946682 the whole document ---	1-6,9
P,A	WO 99 21574 A (CREATIVE BIOMOLECULES INC ;CHARETTE MARC F (US); HIGGINS DENNIS (U) 6 May 1999 (1999-05-06) page 2, line 11 -page 3, line 2 page 28, line 12 -page 30, line 12 claims 4,8,9,13 --- -/--	1-9

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 00/01211

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	CORCORAN JONATHAN ET AL: "Nerve growth factor acts via retinoic acid synthesis to stimulate neurite outgrowth." NATURE NEUROSCIENCE, vol. 2, no. 4, April 1999 (1999-04), pages 307-308, XP000946659 ISSN: 1097-6256 cited in the application the whole document ---	1-6,9
T	CORCORAN JONATHAN ET AL: "The role of retinoic acid receptors in neurite outgrowth from different populations of embryonic mouse dorsal root ganglia." JOURNAL OF CELL SCIENCE, vol. 113, no. 14, July 2000 (2000-07), pages 2567-2574, XP000946689 ISSN: 0021-9533 the whole document -----	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/01211

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
W0 9623070 A	01-08-1996	AU 4763796 A	14-08-1996
		CA 2211142 A	01-08-1996
		EP 0812354 A	17-12-1997
W0 9702030 A	23-01-1997	IT T0950551 A	30-12-1996
		AU 6241096 A	05-02-1997
		EP 0836476 A	22-04-1998
W0 9724116 A	10-07-1997	US 5965606 A	12-10-1999
		AU 710483 B	23-09-1999
		AU 1345097 A	28-07-1997
		BR 9612318 A	28-12-1999
		CA 2241758 A	10-07-1997
		CN 1211180 A	17-03-1999
		CZ 9802069 A	14-04-1999
		EP 0869782 A	14-10-1998
		PL 327627 A	21-12-1998
US 4808630 A	28-02-1989	AU 607961 B	21-03-1991
		AU 1027788 A	21-07-1988
		EP 0279175 A	24-08-1988
		HU 46209 A, B	28-10-1988
		JP 63188622 A	04-08-1988
		PH 25294 A	30-04-1991
W0 9921574 A	06-05-1999	ZA 8800219 A	22-02-1989
		AU 1122099 A	17-05-1999
		EP 1027059 A	16-08-2000